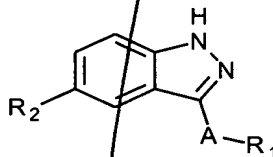


What is claimed is:

1. A compound having the structure:



or a pharmaceutically acceptable salt thereof, wherein:

A is a direct bond, $-(CH_2)_a-$, $-(CH_2)_bCH=CH(CH_2)_c-$, or $-(CH_2)_bC\equiv C(CH_2)_c-$;

R_1 is aryl, heteroaryl or heterocycle fused to phenyl, each being optionally substituted with one to four substituents independently selected from R_3 ;

R_2 is $-R_3$, $-R_4$, $-(CH_2)_bC(=O)R_5$, $-(CH_2)_bC(=O)OR_5$, $-(CH_2)_bC(=O)NR_5R_6$,

$-(CH_2)_bC(=O)NR_5(CH_2)_cC(=O)R_6$, $-(CH_2)_bNR_5C(=O)R_6$,

$-(CH_2)_bNR_5C(=O)NR_6R_7$, $-(CH_2)_bNR_5R_6$, $-(CH_2)_bOR_5$,

$-(CH_2)_bSO_2R_5$ or $-(CH_2)_bSO_2NR_5R_6$;

a is 1, 2, 3, 4, 5 or 6;

b and c are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4;

d is at each occurrence 0, 1 or 2;

R_3 is at each occurrence independently halogen, hydroxy, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl, substituted heterocyclealkyl, $-C(=O)OR_8$, $-C(=O)R_8$, $-C(O)NR_8R_9$, $-C(=O)NR_8OR_9$, $-SO_2NR_8R_9$, $-NR_8SO_2R_9$, $-CN$, $-NO_2$, $-NR_8R_9$, $-NR_8C(=O)R_9$, $-NR_8C(=O)(CH_2)_bOR_9$, $-NR_8C(=O)(CH_2)_bR_9$, $-O(CH_2)_bNR_8R_9$, or heterocycle fused to phenyl;

R_4 is alkyl, aryl, arylalkyl, heterocycle or heterocyclealkyl, each being optionally substituted with one to four substituents independently selected from R_3 , or R_4 is halogen or hydroxy;

R_5 , R_6 and R_7 are the same or different and at each occurrence independently hydrogen, alkyl, aryl, arylalkyl, heterocycle or heterocyclealkyl, wherein each of R_5 , R_6 and R_7 are optionally substituted with one to four substituents independently selected from R_3 ; and

R₈ and R₉ are the same or different and at each occurrence independently hydrogen, alkyl, aryl, arylalkyl, heterocycle, or heterocyclealkyl, or R₈ and R₉ taken together with the atom or atoms to which they are bonded form a heterocycle, wherein each of R₈, R₉, and R₈ and R₉ taken together to form a heterocycle are optionally substituted with one to four substituents independently selected from R₃

with the proviso that:

when A is a direct bond and R₁ is phenyl,

R₂ is not methyl, methoxy, C(=O)CH₃ or C(=O)H;

when A is a direct bond and R₁ is 4-Me-phenyl,

R₂ is not methyl;

when A is a direct bond and R₁ is 4-F-phenyl,

R₂ is not trifluoromethyl;

when A is a direct bond or -C≡C- and R₁ is phenyl,

R₂ is not -COOEt; and

when A is a direct bond and R₁ is 6,7-dimethoxyisoquinolin-1-yl,

R₂ is not hydroxy.

2. The compound of claim 1 wherein:

R₂ is -R₄, -(CH₂)_bC(=O)R₅, -(CH₂)_bC(=O)OR₅, -(CH₂)_bC(=O)NR₅R₆,

-(CH₂)_bC(=O)NR₅(CH₂)_cC(=O)R₆, -(CH₂)_bNR₅C(=O)R₆,

-(CH₂)_bNR₅C(=O)NR₆R₇, -(CH₂)_bNR₅R₆, -(CH₂)_bOR₅, -(CH₂)_bSO_aR₅ or

-(CH₂)_bSO₂NR₅R₆.

3. The compound of claim 1 wherein A is a direct bond.

4. The compound of claim 1 wherein A is -(CH₂)_a-.

5. The compound of claim 1 wherein A is -(CH₂)_bCH=CH(CH₂)_c-.

6. The compound of claim 1 wherein A is -(CH₂)_bC≡C(CH₂)_c-.

7. The compound of claim 1 wherein R₁ is aryl optionally substituted with one to four substituents independently selected from R₃.

8. The compound of claim 1 wherein R_1 is heteroaryl optionally substituted with one to four substituents independently selected from R_3 .

9. The compound of claim 1 wherein R_1 is heterocycle fused to phenyl optionally substituted with one to four substituents independently selected from R_3 .

10. The compound of claim 1 wherein R_2 is $-(CH_2)_bC(=O)R_5$.

11. The compound of claim 1 wherein R_2 is $-(CH_2)_bC(=O)NR_5R_6$.

12. The compound of claim 1 wherein R_2 is $-(CH_2)_bNR_5C(=O)R_6$.

13. The compound of claim 1 wherein R_2 is $-(CH_2)_bNR_5R_6$.

14. The compound of claim 1 wherein R_2 is R_4 .

15. The compound of claim 14 wherein R_4 is substituted alkyl.

16. The compound of claim 14 wherein R_4 is substituted arylalkyl.

17. The compound of claim 14 wherein R_4 is substituted heterocycle.

18. The compound of claim 14 wherein R_4 is 3-triazolyl, optionally substituted at its 5-position with:

(a) a C_1 - C_4 straight or branched chain alkyl group optionally substituted with a hydroxyl, methylamino, dimethylamino or 1-pyrrolidinyl group; or

(b) a 2-pyrrolidinyl group.

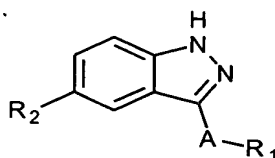
19. The compound of claim 14 wherein R_4 is tetrazole.

20. The compound of claim 14 wherein R_4 is imidazole.

21. A composition comprising the compound of claim 1 and a pharmaceutically acceptable carrier.

22. A method for treating a condition responsive to JNK inhibition, comprising administering to a patient in need thereof an effective amount of a compound having the structure:

5



or a pharmaceutically acceptable salt thereof,

10

wherein:

A is a direct bond, $-(CH_2)_a-$, $-(CH_2)_bCH=CH(CH_2)_c-$, or $-(CH_2)_bC\equiv C(CH_2)_c-$;

R_1 is aryl, heteroaryl or heterocycle fused to phenyl, each being optionally

substituted with one to four substituents independently selected from R_3 ;

15

R_2 is $-R_3$, $-R_4$, $-(CH_2)_bC(=O)R_5$, $-(CH_2)_bC(=O)OR_5$, $-(CH_2)_bC(=O)NR_5R_6$,

$-(CH_2)_bC(=O)NR_5(CH_2)_cC(=O)R_6$, $-(CH_2)_bNR_5C(=O)R_6$,

$-(CH_2)_bNR_5C(=O)NR_6R_7$, $-(CH_2)_bNR_5R_6$, $-(CH_2)_bOR_5$,

$-(CH_2)_bSO_dR_5$ or $-(CH_2)_bSO_2NR_5R_6$;

a is 1, 2, 3, 4, 5 or 6;

20

b and c are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4;

d is at each occurrence 0, 1 or 2;

25

R_3 is at each occurrence independently halogen, hydroxy, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl, substituted heterocyclealkyl, $-C(=O)OR_8$, $-OC(=O)R_8$, $-C(=O)NR_8R_9$, $-C(=O)NR_8OR_9$, $-SO_2NR_8R_9$, $-NR_8SO_2R_9$, $-CN$, $-NO_2$, $-NR_8R_9$, $-NR_8C(=O)R_9$, $-NR_8C(=O)(CH_2)_bOR_9$, $-NR_8C(=O)(CH_2)_bR_9$, $-O(CH_2)_bNR_8R_9$, or heterocycle fused to phenyl;

30

R_4 is alkyl, aryl, arylalkyl, heterocycle or heterocyclealkyl, each being optionally substituted with one to four substituents independently selected from R_3 , or R_4 is halogen or hydroxy;

35

R_5 , R_6 and R_7 are the same or different and at each occurrence independently hydrogen, alkyl, aryl, arylalkyl, heterocycle or heterocyclealkyl, wherein each of R_5 , R_6 and R_7 are optionally substituted with one to four substituents independently selected from R_3 ; and

5 R₈ and R₉ are the same or different and at each occurrence independently hydrogen, alkyl, aryl, arylalkyl, heterocycle, or heterocyclealkyl, or R₈ and R₉ taken together with the atom or atoms to which they are bonded form a heterocycle, wherein each of R₈, R₉, and R₈ and R₉ taken together to form a heterocycle are optionally substituted with one to four substituents independently selected from R₃.

23. The method of claim 22 wherein:

10 R₂ is -R₄, -(CH₂)_bC(=O)R₅, -(CH₂)_bC(=O)OR₅, -(CH₂)_bC(=O)NR₅R₆, -(CH₂)_bC(=O)NR₅(CH₂)_cC(=O)R₆, -(CH₂)_bNR₅C(=O)R₆, -(CH₂)_bNR₅C(=O)NR₆R₇, -(CH₂)_bNR₅R₆, -(CH₂)_bOR₅, -(CH₂)_bSO_dR₅ or -(CH₂)_bSO₂NR₅R₆.

15 24. The method of claim 22 wherein the condition is cancer.

25. The method of claim 22 wherein the condition is rheumatoid arthritis; rheumatoid spondylitis; osteoarthritis; gout; asthma, bronchitis; allergic rhinitis; chronic obstructive pulmonary disease; cystic fibrosis; inflammatory bowel disease; irritable bowel syndrome; mucous colitis; ulcerative colitis; Crohn's disease; Huntington's disease; gastritis; esophagitis; hepatitis; 20 pancreatitis; nephritis; multiple sclerosis; endotoxin shock; lupus erythematosus; Type II diabetes; psoriasis; burn caused by exposure to fire, chemicals or radiation; eczema; dermatitis; skin graft; ischemia; ischemic conditions associated with surgery or traumatic injury; cachexia or angiogenic and proliferative diseases.

25 26. The method of claim 22 wherein the condition is atherosclerosis, restenosis following angioplasty, left ventricular hypertrophy, or myocardial infarction.

27. The method of claim 22 wherein the condition is stroke or ischemic damages of heart, lung, gut, kidney, liver, pancreas, spleen or brain.

30 28. The method of claim 22 wherein the condition is acute or chronic organ transplant rejection, preservation of the organ for transplantation, graft versus host disease or multiple organ failure.

29. The method of claim 22 wherein the condition is epilepsy, Alzheimer's disease, or Parkinson's disease.

30. The method of claim 22 wherein the condition is an immunological response to bacterial or viral infection.

31. The method of claim 22 wherein the condition is solid tumor or cancers of a variety of tissues such as colon, rectum, prostate, liver, lung, bronchus, pancreas, brain, head, neck, stomach, skin, kidney, cervix, blood, larynx, esophagus, mouth, pharynx, urinary bladder, ovary or uterine.

32. The method of claim 22 wherein A is a direct bond.

33. The method of claim 22 wherein A is $-(CH_2)_a-$.

34. The method of claim 22 wherein A is $-(CH_2)_bCH=CH(CH_2)_c-$.

35. The method of claim 22 wherein A is $-(CH_2)_bC\equiv C(CH_2)_c-$.

36. The method of claim 22 wherein R_1 is aryl optionally substituted with one to four substituents independently selected from R_3 .

37. The method of claim 22 wherein R_1 is heteroaryl optionally substituted with one to four substituents independently selected from R_3 .

38. The method of claim 22 wherein R_1 is heterocycle fused to phenyl optionally substituted with one to four substituents independently selected from R_3 .

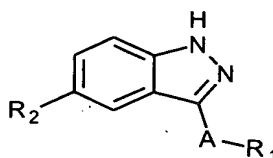
39. The method of claim 22 wherein R_2 is $-(CH_2)_bC(=O)R_5$.

40. The method of claim 22 wherein R_2 is $-(CH_2)_bC(=O)NR_5R_6$.

41. The method of claim 22 wherein R_2 is $-(CH_2)NR_5C(=O)R_6$.

42. The method of claim 22 wherein R_2 is $-(CH_2)_bNR_5R_6$.
43. The method of claim 22 wherein R_2 is R_4 .
- 5 44. The method of claim 43 wherein R_4 is substituted alkyl.
45. The method of claim 43 wherein R_4 is substituted arylalkyl.
46. The method of claim 43 wherein R_4 is substituted heterocycle.
- 10 47. The method of claim 43 wherein R_4 is 3-triazolyl, optionally substituted at its 5-position with:
- (a) a C_1 - C_4 straight or branched chain alkyl group optionally substituted with a hydroxyl, methylamino, dimethylamino or 1-pyrrolidinyl group; or
- 15 (b) a 2-pyrrolidinyl group.
48. The method of claim 43 wherein R_4 is tetrazole.
49. The method of claim 43 wherein R_4 is imidazole.
- 20 50. A method for treating or preventing rheumatoid arthritis; rheumatoid spondylitis; osteoarthritis; gout; asthma, bronchitis; allergic rhinitis; chronic obstructive pulmonary disease; cystic fibrosis; inflammatory bowel disease; irritable bowel syndrome; mucous colitis; ulcerative colitis; Crohn's disease; Huntington's disease; gastritis; esophagitis; hepatitis;
- 25 pancreatitis; nephritis; multiple sclerosis; lupus erythematosus; Type II diabetes; atherosclerosis; restenosis following angioplasty; left ventricular hypertrophy; myocardial infarction; stroke; ischemic damages of heart, lung, gut, kidney, liver, pancreas, spleen and brain; acute or chronic organ transplant rejection; preservation of an organ for transplantation; graft versus host disease; endotoxin shock; multiple organ failure; psoriasis; burn caused by exposure to fire, chemicals, or
- 30 radiation; eczema; dermatitis; skin graft; ischemia; ischemic conditions associated with surgery or traumatic injury; epilepsy; Alzheimer's disease; Parkinson's disease; immunological response to bacterial or viral infection; cachexia; angiogenic and proliferative diseases; solid tumor; and cancers of a variety of tissues such as colon, rectum, prostate, liver, lung, bronchus, pancreas, brain, head, neck, stomach, skin, kidney, cervix, blood, larynx, esophagus, mouth, pharynx, urinary
- 35

bladder, ovary, or uterine comprising administering to a patient in need of such treatment or prevention an effective amount of a compound having the structure:



or a pharmaceutically acceptable salt thereof,

10 wherein:

A is a direct bond, $-(CH_2)_a-$, $-(CH_2)_bCH=CH(CH_2)_c-$, or $-(CH_2)_bC\equiv C(CH_2)_c-$;

R_1 is aryl, heteroaryl or heterocycle fused to phenyl, each being optionally substituted with one to four substituents independently selected from R_3 ;

15 R_2 is $-R_3$, $-R_4$, $-(CH_2)_bC(=O)R_5$, $-(CH_2)_bC(=O)OR_5$, $-(CH_2)_bC(=O)NR_5R_6$, $-(CH_2)_bC(=O)NR_5(CH_2)_cC(=O)R_6$, $-(CH_2)_bNR_5C(=O)R_6$, $-(CH_2)_bNR_5C(=O)NR_6R_7$, $-(CH_2)_bNR_5R_6$, $-(CH_2)_bOR_5$, $-(CH_2)_bSO_dR_5$ or $-(CH_2)_bSO_2NR_5R_6$;

a is 1, 2, 3, 4, 5 or 6;

20 b and c are the same or different and at each occurrence independently selected from 0, 1, 2, 3 or 4;

d is at each occurrence 0, 1 or 2;

25 R_3 is at each occurrence independently halogen, hydroxy, carboxy, alkyl, alkoxy, haloalkyl, acyloxy, thioalkyl, sulfinylalkyl, sulfonylalkyl, hydroxyalkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heterocycle, substituted heterocycle, heterocyclealkyl, substituted heterocyclealkyl, $-C(=O)OR_8$, $-OC(=O)R_8$, $-C(=O)NR_8R_9$, $-C(=O)NR_8OR_9$, $-SO_2NR_8R_9$, $-NR_8SO_2R_9$, $-CN$, $-NO_2$, $-NR_8R_9$, $-NR_8C(=O)R_9$, $-NR_8C(=O)(CH_2)_bOR_9$, $-NR_8C(=O)(CH_2)_bR_9$, $-O(CH_2)_bNR_8R_9$, or heterocycle fused to phenyl;

30 R_4 is alkyl, aryl, arylalkyl, heterocycle or heterocyclealkyl, each being optionally substituted with one to four substituents independently selected from R_3 , or R_4 is halogen or hydroxy;

35 R_5 , R_6 and R_7 are the same or different and at each occurrence independently hydrogen, alkyl, aryl, arylalkyl, heterocycle or heterocyclealkyl, wherein each of R_5 , R_6 and R_7 are optionally substituted with one to four substituents independently selected from R_3 ; and

R_8 and R_9 are the same or different and at each occurrence independently hydrogen, alkyl, aryl, arylalkyl, heterocycle, or heterocyclealkyl, or R_8 and R_9 taken together with the atom or atoms to which they are bonded form a heterocycle, wherein each of R_8 , R_9 , and R_8 and R_9 taken together to form a heterocycle are optionally substituted with one to four substituents independently selected from R_3 .

51. The method of claim 50 wherein:

R_2 is $-R_4$, $-(CH_2)_bC(=O)R_5$, $-(CH_2)_bC(=O)OR_5$, $-(CH_2)_bC(=O)NR_5R_6$, $-(CH_2)_bC(=O)NR_5(CH_2)_cC(=O)R_6$, $-(CH_2)_bNR_5C(=O)R_6$, $-(CH_2)_bNR_5C(=O)NR_6R_7$, $-(CH_2)_bNR_5R_6$, $-(CH_2)_bOR_5$, $-(CH_2)_bSO_aR_5$ or $-(CH_2)_bSO_2NR_5R_6$.

52. The method of claim 50 wherein A is a direct bond.

53. The method of claim 50 wherein A is $-(CH_2)_a-$.

54. The method of claim 50 wherein A is $-(CH_2)_bCH=CH(CH_2)_c-$.

55. The method of claim 50 wherein A is $-(CH_2)_bC\equiv C(CH_2)_c-$.

56. The method of claim 50 wherein R_1 is aryl optionally substituted with one to four substituents independently selected from R_3 .

57. The method of claim 50 wherein R_1 is heteroaryl optionally substituted with one to four substituents independently selected from R_3 .

58. The method of claim 50 wherein R_1 is heterocycle fused to phenyl optionally substituted with one to four substituents independently selected from R_3 .

59. The method of claim 50 wherein R_2 is $-(CH_2)_bC(=O)R_5$.

60. The method of claim 50 wherein R_2 is $-(CH_2)_bC(=O)NR_5R_6$.

61. The method of claim 50 wherein R_2 is $-(CH_2)NR_5C(=O)R_6$.
61. The method of claim 50 wherein R_2 is $-(CH_2)_bNR_5R_6$.
- 5 63. The method of claim 50 wherein R_2 is R_4 .
64. The method of claim 63 wherein R_4 is substituted alkyl.
65. The method of claim 63 wherein R_4 is substituted arylalkyl.
- 10 66. The method of claim 63 wherein R_4 is substituted heterocycle.
67. The method of claim 63 wherein R_4 is 3-triazolyl, optionally substituted at its 5-position with:
- 15 (a) a C_1 - C_4 straight or branched chain alkyl group optionally substituted with a hydroxyl, methylamino, dimethylamino or 1-pyrrolidinyl group; or
- (b) a 2-pyrrolidinyl group.
68. The method of claim 63 wherein R_4 is tetrazole.
- 20 69. The method of claim 63 wherein R_4 is imidazole.
70. The compound of claim 1, wherein $-A-R_1$ is phenyl, optionally substituted with one to four substituents independently selected from halogen, alkoxy, $-NR_8C(=O)R_9$, $-C(=O)NR_8R_9$, and $-O(CH_2)_bNR_8R_9$, wherein b is 2 or 3.
- 25 71. The compound of claim 1, wherein R_2 is $-(CH_2)_bC(=O)NR_5R_6$, $-(CH_2)_bNR_5C(=O)R_6$, 3-triazolyl or 5-tetrazolyl, wherein b is 0.
- 30 72. The compound of claim 1, wherein R_2 is 3-triazolyl or 5-tetrazolyl.
73. The compound of claim 1, wherein:
- (a) $-A-R_1$ is phenyl, optionally substituted with one to four substituents independently selected from halogen, alkoxy, $-NR_8C(=O)R_9$, $-C(=O)NR_8R_9$, and $-O(CH_2)_bNR_8R_9$, wherein b is 2 or 3; and
- 35

(b) R_2 is $-(CH_2)_bC(=O)NR_5R_6$, $-(CH_2)_bNR_5C(=O)R_6$, 3-triazolyl or 5-tetrazolyl, wherein b is 0.

74. The compound of claim 1, wherein

(a) $-A-R_1$ is phenyl, optionally substituted with one to four substituents independently selected from halogen, alkoxy, $-NR_8C(=O)R_9$, $-C(=O)NR_8R_9$, and $-O(CH_2)_bNR_8R_9$, wherein b is 2 or 3; and

(b) R_2 is 3-triazolyl or 5-tetrazolyl.

10 75. The method of claim 22, wherein $-A-R_1$ is phenyl, optionally substituted with one to four substituents independently selected from halogen, alkoxy, $-NR_8C(=O)R_9$, $-C(=O)NR_8R_9$, and $-O(CH_2)_bNR_8R_9$, wherein b is 2 or 3.

15 76. The method of claim 22, wherein R_2 is $-(CH_2)_bC(=O)NR_5R_6$, $-(CH_2)_bNR_5C(=O)R_6$, 3-triazolyl or 5-tetrazolyl, wherein b is 0.

77. The method of claim 22, wherein R_2 is 3-triazolyl or 5-tetrazolyl.

78. The method of claim 22, wherein:

20 (a) $-A-R_1$ is phenyl, optionally substituted with one to four substituents independently selected from halogen, alkoxy, $-NR_8C(=O)R_9$, $-C(=O)NR_8R_9$, and $-O(CH_2)_bNR_8R_9$, wherein b is 2 or 3; and

(b) R_2 is $-(CH_2)_bC(=O)NR_5R_6$, $-(CH_2)_bNR_5C(=O)R_6$, 3-triazolyl or 5-tetrazolyl, wherein b is 0.

25

79. The method of claim 22, wherein

(a) $-A-R_1$ is phenyl, optionally substituted with one to four substituents independently selected from halogen, alkoxy, $-NR_8C(=O)R_9$, $-C(=O)NR_8R_9$, and $-O(CH_2)_bNR_8R_9$, wherein b is 2 or 3; and

30 (b) R_2 is 3-triazolyl or 5-tetrazolyl.

80. The method of claim 50, wherein $-A-R_1$ is phenyl, optionally substituted with one to four substituents independently selected from halogen, alkoxy, $-NR_8C(=O)R_9$, $-C(=O)NR_8R_9$, and $-O(CH_2)_bNR_8R_9$, wherein b is 2 or 3.

35

81. The method of claim 50, wherein R_2 is $-(CH_2)_bC(=O)NR_5R_6$, $-(CH_2)_bNR_5C(=O)R_6$, 3-triazolyl or 5-tetrazolyl, wherein b is 0.

5 82. The method of claim 50, wherein R_2 is 3-triazolyl or 5-tetrazolyl.

83. The method of claim 50, wherein:

(a) $-A-R_1$ is phenyl, optionally substituted with one to four substituents independently selected from halogen, alkoxy, $-NR_8C(=O)R_9$, $-C(=O)NR_8R_9$, and $-O(CH_2)_bNR_8R_9$, wherein b is 2 or 3; and

10 (b) R_2 is $-(CH_2)_bC(=O)NR_5R_6$, $-(CH_2)_bNR_5C(=O)R_6$, 3-triazolyl or 5-tetrazolyl, wherein b is 0.

84. The method of claim 50, wherein:

15 (a) $-A-R_1$ is phenyl, optionally substituted with one to four substituents independently selected from halogen, alkoxy, $-NR_8C(=O)R_9$, $-C(=O)NR_8R_9$, and $-O(CH_2)_bNR_8R_9$, wherein b is 2 or 3; and

(b) R_2 is 3-triazolyl or 5-tetrazolyl.

20 85. The compound of claim 18 wherein R_4 is methyl, n-propyl, isopropyl, 1-hydroxyethyl, 3-hydroxypropyl, methylaminomethyl, dimethylaminomethyl, 1-(dimethylamino)ethyl, 1-pyrrolidinylmethyl or 2-pyrrolidinyl.

25 86. The method of claim 47 wherein R_4 is methyl, n-propyl, isopropyl, 1-hydroxyethyl, 3-hydroxypropyl, methylaminomethyl, dimethylaminomethyl, 1-(dimethylamino)ethyl, 1-pyrrolidinylmethyl or 2-pyrrolidinyl.

30 87. The method of claim 67 wherein R_4 is methyl, n-propyl, isopropyl, 1-hydroxyethyl, 3-hydroxypropyl, methylaminomethyl, dimethylaminomethyl, 1-(dimethylamino)ethyl, 1-pyrrolidinylmethyl or 2-pyrrolidinyl.